DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 18-225/S-022

Hoffmann-LaRoche Inc.
Attention: Ms. Lynn DeVenezia-Tobias
340 Kingsland Street
Nutley, NJ 07110-1199

Dear Ms. DeVenezia-Tobias:

Please refer to your supplemental new drug application dated March 18, 2003 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Bumex (bumetanide) 0.5, 1 & 2 mg Tablets.

This "Changes Being Effected" supplemental new drug application provides for electronic final printed labeling revised by the deletion of the Bumex Injection information from the Tablet/Injection package insert as follows:

1. The word "INJECTION" was deleted from the beginning of the package insert.

2. Under the DESCRIPTION section, the following text was deleted from the first paragraph:

   > Also as 2-mL vials, 4-mL vials and 10-mL vials (0.25 mg/mL) for intravenous or intramuscular injection as a sterile solution, each 2 mL of which contains 0.5 mg (0.25 mg/mL) bumetanide compounded with 0.85% sodium chloride and 0.4% ammonium acetate as buffers; 0.01% edetate disodium; 1% benzyl alcohol as preservative and pH adjusted to approximately 7 with sodium hydroxide.

3. Under the DOSAGE AND ADMINISTRATION/Parenteral Administration sub-section, the following paragraph was deleted:

   > The usual initial dose is 0.5 mg to 1 mg intravenously or intramuscularly. Intravenous administration should be given over a period of 1 to 2 minutes. If the response to an initial dose is deemed insufficient, a second or third dose may be given at intervals of 2 to 3 hours, but should not exceed a daily dosage of 10 mg.

4. Under the DOSAGE AND ADMINISTRATION section, the following sub-section and text was deleted:

   > Miscibility and Parenteral Solutions
   > The compatibility tests of Bumex injection (0.25 mg/mL, 2 mL vials) with 5% dextrose in water, 0.9% sodium chloride and lactated Ringer's solution in both glass and plasticized PVC (Viaflex) containers have shown no significant absorption effect with either containers, nor a measurable loss of potency due to degradation of the drug. However, solutions should be freshly prepared and used within 24 hours.
   >
   > Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.

5. Under the HOW SUPPLIED section:

   - The follow text was deleted:

     > Vials (0.25 mg/mL), 2 mL, boxes of 10 (NDC 0004-1968-01); 4 mL, boxes of 10 (NDC 0004-1969-01); 10 mL, boxes of 10 (NDC 0004-1970-01).

   - The statement "Store all tablets and vials at 59° to 86°F (15° to 30°C)." was revised to read "Store tablets at 59° to 86°F (15° to 30°C)."

In addition the following editorial changes are noted:

1. The tradename "Bumex" was changed to "bumetanide" in multiple places throughout the labeling.

2. Under the DOSAGE AND ADMINISTRATION/Parenteral Administration section, the word "Bumex" was replaced with "bumetanide injection."

3. Manufacture code and revised date are updated.

We have completed our review of this supplemental new drug application, as amended, and it is approved effective on the date of this letter for use as recommended in the final printed labeling (FPL) included in your submission dated March 18, 2003.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please call:

Mr. Daryl Allis
Regulatory Health Project Manager
(301) 594-5309

Sincerely,

{See appended electronic signature page}

Douglas C. Throckmorton, M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation 1
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Doug Throckmorton
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